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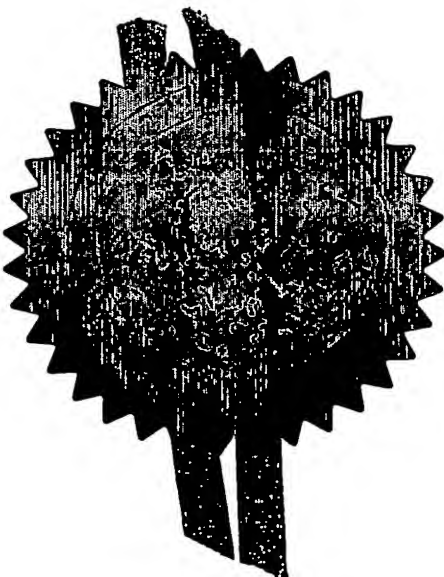
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Dated 21 July 2004

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JPP217

2. Patent application number

(The Patent Office will fill in this part)

0315726.0

04 JUL 2003

3. Full name, address and postcode of the or of each applicant (underline all surnames)

Petlife International Limited
Minster House
Bury St. Edmunds
Suffolk
IP33 3SP

Patents ADP number (*if you know it*)

If the applicant is a corporate body, give the country/state of its incorporation

8664617001

4. Title of the invention

Improvements In Or Relating To Organic Material

5. Name of your agent (*if you have one*)

Barker Brettell

"Address for service" in the United Kingdom to which all correspondence should be sent (*including the postcode*)

10-12 Priests Bridge
LONDON
SW15 5JE

Patents ADP number (*if you know it*)

7442494003

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Number of earlier application

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Yes

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Description 11

Claim(s) 2

Abstract

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Signature

Barker Brettell
Barker Brettell

Date

04 July 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

James Peel

Tel: 020 8392 2234

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IMPROVEMENTS IN OR RELATING TO ORGANIC MATERIAL

The invention relates to an improved barrier formulation and a method for its manufacture.

5

Barrier creams or lotions are useful in a number of applications, particularly where protective clothing cannot be used or is not appropriate. This is to solve the problems of contact dermatitis and hospital acquired infection.

10

Contact dermatitis can arise for workers in certain environments such as hairdressing, health care etc. It is generally caused by substances that come into contact with the skin. A substance that causes allergic contact dermatitis is called an "allergen". If a person is allergic to an allergen, then contact between that allergen and the person's skin can produce itching and blisters (allergic contact dermatitis). Allergic contact dermatitis is not usually caused by irritants such as acid, alkali, solvents, strong soap or detergent. However some chemicals are both irritants and allergens. Examples of known allergens include nickel, rubber, para-phenylene-diamine hair dye, neomycin, chromates, and plant products.

20

The problem with existing barrier formulations is that they do not last particularly long before losing their properties and have to be frequently re-applied. Therefore they do not provide complete protection against allergens. A way of ameliorating this problem has been sought.

25

Hospital acquired infection (HAI) is a major cause for concern in the clinical setting. In the UK, it is estimated that approximately 9% of in-patients have a HAI at any one time, which equates to at least 300,000 infections per annum (National Audit Office, 'The Management and Control of Hospital Acquired Infection in acute NHS Trusts in England',

30

London: Stationery Office 2000). The costs associated with treating HAI are difficult to measure, however results from a recent study undertaken by the London School of Hygiene and Tropical Medicine and the Central Public Health Laboratory, suggest that HAI may be costing the NHS as much as £1 billion per year (*ibid*). It is not possible to prevent all HAIs, however, the National Audit Office report suggests that HAIs could be reduced by up to 15% through better application of existing knowledge and realistic and effective infection control practices (*ibid*).

10 Hand hygiene is one of the basic components of any infection control program and is possibly the most important factor in preventing HAI. Indeed, outbreaks originating from a common source have been traced to contaminated hands of health care workers (HCW) (Boyce JM, Potter-Bynoe G, Opal SM *et al* "A Common-Source Outbreak of *Staphylococcus*
15 *epidermidis* Infections among Patients undergoing Cardiac Surgery Journal of Infectious Diseases 1990; 161: 493-499). In a recent survey, it was demonstrated that HCW understand the importance of hand hygiene as a means of preventing infection and are in favour of interventions that make hand hygiene easier (Harris AD, Samore MH, Nafziger R *et al* "A
20 Survey on Hand Washing Practices and Opinions of Healthcare Workers" Journal of Hospital Infection 2000; 45:318-21). However, studies have also consistently demonstrated that HCW frequently do not wash their hands and compliance rates are low (Pittet D, Mourouga P, Perneger TV "Compliance with Handwashing in a Teaching Hospital" *Ann Intern Med*
25 1999; 130: 126-130).

The recent EPIC evidence based guidelines on hand hygiene, commissioned by the Department of Health (Pratt RJ, Pellowe C, Loveday HP *et al* "The EPIC Project: Developing National Evidence-Based Guidelines for Preventing Healthcare Associated Infections, Phase
30 I: Guidelines for Preventing Hospital Acquired Infections" *Journal of*

Hospital Infection 2001; 47 (suppl): S1-82) recommends that formal hand washing with soap and water should be undertaken by HCW when hands are visibly soiled or contaminated, and alcohol-glycerol hand rub used between patients. These methods of hand hygiene require adequate
5 cleansing facilities, including suitably located sinks and gel dispensers of sufficient numbers, which may not always be present within the clinical setting. In view of the lack of compliance with hand hygiene and despite many initiatives, new ways of ameliorating this problem have been sought.

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According to the invention there is provided a barrier formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound wherein the viscosity of the formulation is 20000 cps or less.

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According to the invention there is also provided a method of manufacturing a formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound which method comprises the steps of:

20

- (a) preparing an oil phase containing a silicone compound;
- (b) preparing an aqueous phase;
- (c) mixing the oil phase and the aqueous phase together;
- (d) neutralising the mixture with a neutralising agent.

25

The formulation according to the invention has been found to act as an effective skin barrier to irritants and/or allergens. In particular it has been found to be possible to apply concentrated sulphuric acid to the skin of a person which has been pre-treated with the formulation according to the invention with no ill effects to the person's skin.

30

The silicone compound is preferably dimethicone, a silicone fluid, a silicone emulsion, a dimethicone cross polymer, a polydimethylsiloxane. More preferably it is a dimethicone. The formulation according to the invention preferably comprises from 0.1 to 10% of the silicone
5 compound, more preferably from 0.5 to 5% by weight, most preferably from 1% to 2% by weight.

The formulation according to the invention is preferably in the form of a lotion in order to be easy to apply and to dispense, particularly in a
10 hospital environment. The viscosity of the formulation is more preferably from 1000 to 20000 cps, most preferably it is from 1000 to 5000 cps.

The formulation according to the invention preferably comprises an active ingredient. The active ingredient may be included in the oil or water
15 phase depending on in which phase it has greater solubility. Preferably the active ingredient is a chemical or physical sun protection agent (e.g. ethylhexyl methoxycinnamate, 4-methylbenzylidene camphor, octyldimethyl PABA), an insect repellent (for example diethyltoluamide (DEET) or Merck Insect Repellent 3535 (trade name)), an anti-bacterial
20 agent (e.g. triclosan), an anti-fungal agent, a non-steroidal anti-inflammatory drug (e.g. ibuprofen, aspirin, diclofenac), and/or a steroid (e.g. hydrocortisone). The active ingredient is preferably present in an amount from 0.5 to 10% by weight of the formulation, preferably from 1 to 5% by weight, more preferably about 2% by weight.

25

~~In the process of the invention, the water phase is preferably added to the~~
oil phase to obtain an oil-in-water emulsion. It has been found that the formulation according to the invention has greater efficacy when it is in the form of an oil-in-water emulsion.

30

The addition of a neutralising agent to the mixture of oil phase and water phase is critical since the agent can only neutralise following the emulsification. This reaction not only adjusts the pH but also the viscosity of the finished product. It is particularly important when the formulation contains a carbomer as it is the carbomer which needs to be neutralised.

A suitable neutralising agent for use in the invention is an alkaline agent, preferably triethanolamine, sodium hydroxide or potassium hydroxide. Triethanolamine is the preferred neutralising agent.

The formulation according to the invention optionally further comprises an emollient, (such as jojoba oil, avocado oil, sunflower oil, kukui nut oil sweet almond oil, coconut oil, apricot kernel oil, castor oil, emu oil walnut oil and/or aloe vera), a thickener (for example cetyl palmitate or a carbomer or other gelling agent), an excipient (e.g. a glycol or alcohol, especially mono-propylene glycol), a preservative (for example Nipastat (Trade Mark), parabens, phenoxyethanol, a isothiazolinone, especially Phenonip (Trade Name), Nipasol (Trade Name), Nipagin (Trade Name), Euxyl K100 (Trade Name)), a fragrance, an emulsifier (especially a stearate derivative e.g. glyceryl monostearate), a neutralising agent (e.g. triethanolamine) and/or water.

The invention will now be illustrated with reference to the following Examples which are not intended to limit the scope of protection obtained.

EXAMPLE 1

A barrier formulation having the ingredients listed in Table 1 was prepared as follows.

TABLE 1

Materials	Amount/wt%	Phase
Castor oil	2.00	A
Stearic acid	6.00	
GMS SE	2.00	
Cetyl Palmitate	1.00	
Silicone fluid	1.00	
Nipastat	0.20	
Jojoba oil	0.10	
Liquid paraffin	0.10	
MPG	10.00	B
Triethanolamine	1.55	
Hot water @65°C	39.65	
Carbopol	5.00	
Triclosan	0.50	C
Aloe vera	0.50	D
Fragrance	0.15	
Cold water	30.25	E

Wherein GMS SE is glyceryl stearate manufactured by Stepan Company, Nipastat is a preservative product containing methyl paraben, butyl paraben, ethyl paraben, propyl paraben and isobutylparaben manufactured by Clariant UK Ltd, MPG is the excipient monopropylene glycol

The ingredients of phase A were melted together at temperature 60°C. The ingredients of phase B were mixed together using a Silverson High Shear Mixer. Phase C was added to phase A and stirred until dissolved. Phase B was then added to phase A. Phase D was then added and mixed using a Silverson High Shear Mixer. Phase E was also added while mixing.

EXAMPLE 2

A barrier formulation having the ingredients listed in Table 2 was prepared as follows.

TABLE 2

Materials	Amount/wt%	Phase
Castor oil	2.0	A
Stearic acid	1.5	
GMS SE	0.5	
Cetyl Palmitate	0.5	
Silicone fluid	1.0	
Nipastat	0.2	
Jojoba oil	0.1	
Liquid paraffin	0.1	
Triclosan	1.0	B
Hot water @ 60°C	80.4	C
Carbopol (5%)	2.0	
Alge vera 10.1	0.5	
MPG	10.0	
Triethanolamine	0.2	D

The ingredients of phase A were melted together at temperature 70°C until the phase was clear. The ingredients of phase C were mixed together using a Silverson High Shear Mixer. Phase B was added to phase A and stirred until dissolved. Phase C was then added to phase A. Phase D was then added and mixed using a Silverson High Shear Mixer.

A barrier formulation having the ingredients listed in Table 3 was prepared as follows.

5

TABLE 3

Materials	Amount/wt%	Phase
Castor oil	2.0	A
Stearic acid	1.5	
GMS SE	0.5	
Cetyl Palmitate	0.5	
Silicone fluid	1.0	
Nipastat	0.2	
Jojoba oil	0.1	
Liquid paraffin	0.1	
Triclosan	2.0	B
MPG	10.0	C
Hot water @ 60°C	79.4	
Carbopol	2.0	
Aloe vera	0.5	
Triethanolamine	0.2	D

The ingredients of phase A were melted together at temperature 65°C until clear. The ingredients of phase C were mixed together using a
 10 Silverson High Shear Mixer. Phase B was added to phase A and stirred
 until dissolved. Phase C was then added to phase A. Phase D was then
 added and mixed using a Silverson High Shear Mixer.

EXAMPLE 4

15

The bactericidal efficacy of the formulation prepared in Example 2 was tested over a 4-hour period on the hands of volunteers. In addition, it was investigated whether repeated applications of soap and water, 4% (w/v) chlorhexidine gluconate (Hydrex) (Adams Healthcare, Leeds, UK) and 70% (v/v) isopropanol (Guest Medical, Kent, UK) to the hands, affected the efficacy of the cream. Five volunteers participated in the study, four of which applied the formulation prepared in Example 2 to their hands. A 2cm² area was designated on the left hand of each volunteer and 50 µl of *Staphylococcus epidermidis* NCTC 9865 at a concentration of approximately 1 x 10⁴ cfu/mL was applied and allowed to dry. *S. epidermidis* NCTC 9865 was selected as an indicator microorganism as it produces a red pigment when grown on nutrient agar.

At 1 hour, each 2cm² section was swabbed and cultured directly onto nutrient agar (Oxoid Ltd, Basingstoke, UK). Three volunteers then washed their hands thoroughly with either soap and water, 4% chlorhexidine gluconate or 70% isopropanol. All plates were incubated at 37°C in air for 48 hours. This process was repeated over a four-hour period at hourly intervals and on two consecutive days. The mean numbers of viable *S. epidermidis* NCTC 9865, recovered from the hands of the volunteers are shown in Table 4.

TABLE 4

Colony forming units of *S. epidermidis* NCTC 9865 recovered from a 2cm² area of skin on the hands of volunteers.

Loading inoculum	Sampling time (hrs)	Control	No washing	Soap/water	4% chlorhexidine gluconate	70% isopropanol
4.4x10 ² (0 hours)	1	3.8x10 ²	0	0	0	1
2.7x10 ² (1 hour)	2	2x10 ²	0	0	0	3
3.6x10 ² (2 hours)	3	3.5x10 ²	0	0	0	1
3.2x10 ² (3 hours)	4	2.9x10 ²	1	0	0	13

The results show that the formulation of Example 2 retained its antibacterial activity over a 4-hour period when challenged with between 3.2×10^2 and 4.4×10^2 cfu of *S. epidermidis* NCTC 9865. Three applications of soap and water, and 4% chlorhexidine gluconate to the hands during the study period did not affect the bactericidal activity of the formulation. Following a third application of 70% isopropanol, 13 cfu of *S. epidermidis* NCTC 9865 was recovered at 4 hours from one volunteer, however this still represented a 3.1×10^2 cfu reduction in viable microorganisms compared to the loading inoculum.

10

The results of this preliminary investigation demonstrate the usefulness of the formulation according to the invention as an effective antimicrobial barrier cream.

CLAIMS

1. A barrier formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound wherein the viscosity of the formulation is 20000 cps or less.
5
2. A formulation as defined in Claim 1 wherein the silicone compound is dimethicone, a silicone fluid, a silicone emulsion, a dimethicone cross polymer, a polydimethylsiloxane, preferably it is a dimethicone.
10
3. A formulation as defined in Claim 1 or Claim 2 which comprises from 0.1 to 10% of the silicone compound, more preferably from 0.5 to 5% by weight, most preferably from 1% to 2% by weight.
- 15 4. A formulation as defined in any one of the preceding Claims which comprises an active ingredient.
5. A formulation as defined in Claim 4 wherein the active ingredient is a chemical or physical sun protection agent, an insect repellent, an anti-bacterial agent, an anti-fungal agent, a non-steroidal anti-inflammatory drug, and/or a steroid.
20
6. A formulation as defined in Claim 5 wherein the active ingredient is present in an amount from 0.5 to 10% by weight of the formulation, preferably from 1 to 5% by weight, more preferably about 2% by weight.
25
7. A formulation as defined in any one of the preceding Claims which comprises an emollient, a thickener, an excipient, a preservative, a fragrance, an emulsifier, a neutralising agent and/or water.

8. A method of manufacturing a formulation comprising an emulsion having at least an oil phase and an aqueous phase wherein the oil phase comprises a silicone compound which method comprises the steps of:

- 5 (a) preparing an oil phase containing a silicone compound;
- (b) preparing an aqueous phase;
- (c) mixing the oil phase and the aqueous phase together;
- (d) neutralising the mixture with a neutralising agent.

9. A method as defined in Claim 8 wherein the water phase is added
10 to the oil phase to obtain an oil-in-water emulsion.

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